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Guidance for Industry

The Administrative New Animal Drug Application Process

DRAFT GUIDANCE

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This draft guidance describes the Center for Veterinary Medicine's Administrative New Animal Drug Application process.

Comments and suggestions regarding this draft document should be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. Submit electronic comments to http://www.fda.gov/dockets/ecomments. All comments should be identified with Docket Number 02D-0449.

For questions regarding this draft guidance document, contact Gail Schmerfeld, Center for Veterinary Medicine (HFV- 100), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 301-827-1796 (e-mail: gschmer1@cvm.fda.gov)

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III. The Administrative NADA process

Definition: An "Administrative NADA" is a new animal drug application that is submitted after all of the technical sections that fulfill the requirements for the approval of the new animal drug under 21 CFR 514.1 have been reviewed by CVM and CVM has issued a technical section complete letter for each of those technical sections.

The Phased Review Process

A sponsor may submit data or information in support of a technical section, or may submit a complete technical section, of the NADA for review during the investigation of the new animal drug, i.e., for phased review. The same requirements under 21 CFR 514.1 apply to all NADAs whether for phased review or not. Phasing of NADA submissions is a voluntary program.[1] The option to phase the review of data submissions applies to all original NADAs and to supplemental NADAs and can be exercised up to the point at which the sponsor submits an NADA or supplemental NADA. Applicants making submissions relating to abbreviated NADAs and supplements should contact the Generic Animal Drug Team to discuss whether phased review is appropriate for their particular generic new animal drug.

If a sponsor exercises the option to use the phased review process:

A. Submissions relating to technical sections should be submitted during the investigation of the new animal drug and filed in an Investigational New Animal Drug (INAD) file established by CVM for the new animal drug.

B. Each submission should contain information and data relating to only one technical section and should be under a separate cover. Sponsors are encouraged to contact the reviewing Division regarding what information and data should be submitted together.

C. Each submission relating to a different technical section should be bound separately and should include a cover letter, a table of contents, a summary, and other information pertinent to the review of the particular section. The envelope in which a submission is mailed should be addressed to the Document Control Unit, HFV-199, CVM, FDA, 519 Standish Place, Rockville, MD 20855. The cover letter should: (1) at the top identify the submission as a "Phased Submission;" (2) be addressed to the Division or Staff Director responsible for the evaluation of the technical section; (3) briefly describe the purpose of

[1] In deciding whether to seek approval of a new animal drug under phased review or under the traditional review process by submitting all data together, a sponsor should consider all advantages and disadvantages of each mechanism for approval before submitting data for CVM's review. For example, a sponsor should consider whether seeking approval of a new animal drug under phased review will affect the extension of a patent term. See the discussion in section V. of this guidance.

the submission and the information contained in it, including reference to any pertinent previous correspondence between CVM and the sponsor; (4) reference or attach any pertinent documentation regarding previous agreements or understandings between the sponsor and CVM; (5) identify persons the agency may contact regarding any specifics of the submission; and/or (6) convey any other information the sponsor considers important or necessary to facilitate the review of the submission.

D. There are potentially eight technical sections: Chemistry, Manufacturing, and Controls; Effectiveness; Target Animal Safety; Human Food Safety; Environmental Impact; Labeling; Freedom of Information (FOI) Summary; and, All Other Information. These technical sections are described briefly below. Additionally, the FOI Summary is described in greater detail in 21 CFR § 514.11(e)(2) and each of the other technical sections is described in greater detail in 21 CFR § 514.1.

(1) The **Chemistry, Manufacturing, and Controls** section should contain complete information regarding the manufacture of the new animal drug active ingredient and the new animal drug product. It should include information on personnel, facilities, components and composition, manufacturing procedures, analytical specifications and methods, control procedures, stability, containers and closures, Good Manufacturing Practice (GMP) compliance, and many other aspects of the chemistry and manufacturing processes.

(2) The **Effectiveness** section must contain full reports of all studies that show whether or not the new animal drug is effective for its intended use. 21 CFR § 514.1(b)(8)(i). This section should include both studies with controls and studies without controls conducted by or on behalf of the sponsor or available to the sponsor by right of reference. References and authorizations, if appropriate, to other applications or documents containing information regarding effectiveness of the new animal drug should also be included in this section of the application. Section 512(d)(1)(E) of the Act, 21 USC § 360b(d)(1)(E), provides that CVM must refuse to approve an NADA unless the sponsor demonstrates by substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

(3) The **Target Animal Safety** section must contain full reports of all studies that show whether or not the new animal drug is safe to the target species. 21 CFR § 514.1(b)(8)(i). All studies should include those studies conducted by or on behalf of the sponsor or available to the sponsor by right of reference. References and authorizations, if appropriate, to other applications or documents containing information regarding safety of the new animal drug should also be included in this section of the application.

(4) The **Human Food Safety** section is submitted only for applications for new animal drugs intended for use in species that are used for human food (food-producing animals). This section must, by regulation, 21 CFR § 514.1(b)(7), include a description of practicable methods for determining the quantity, if any, of the new animal

drug in or on food, and any substance formed in or on food because of its use, and the proposed tolerance or withdrawal period or other use restrictions to ensure that the proposed use of the drug will be safe. This section should also contain any data relating to residue toxicology (including the impact of residues on human intestinal microflora), residue chemistry, and, if the new animal drug has anti-infective properties, microbial food safety. When it becomes final, see CVM draft guidance #52, "Microbiological Testing of Antimicrobial Drug Residues in Food."

(5) The **Environmental Impact** section must, by regulation, 21 CFR § 514.1(b)(14), contain either an environmental assessment (EA) under 21 CFR § 25.40, or a request for categorical exclusion under 21 CFR § 25.30 or 25.33. Under 21 CFR § 25.15(a), a claim of categorical exclusion must include a statement of compliance with the categorical exclusion criteria and must state that to the sponsor's knowledge, no extraordinary circumstances exist. "Environmental Impact Considerations" and directions for preparing an EA can be found in 21 CFR Part 25.

(6) The **Labeling** section should include facsimile copies of container labels, package inserts and any other labeling that will be used with the products. For medicated feeds, copies of representative labeling for the Type B and Type C medicated feeds, referred to as "Blue Bird" labeling, should also be included. Facsimile labeling is nearly final labeling that adequately reproduces the package size (actual or to scale); graphics; pictures; type size, font, and color of text; and, the substance of the text to demonstrate to the reviewing Division that the final printed labeling will be in compliance with applicable regulations. Labeling should address any user safety concerns identified during the review process. See 21 U.S.C. § 502(f)(2).

(7) The completed **FOI Summary** should include the specific language relevant to a technical section that was agreed upon during the review of the individual technical section (e.g., the tolerance and withdrawal time for a new animal drug intended for use in food-producing animals) and should be accepted by the Division responsible for the evaluation of the target animal safety technical section. For further information on FOI summaries, see 21 CFR 514.11(e)(2)(ii).

(8) The **All Other Information** section must include all other information, not included in any of the other technical sections, that is pertinent to an evaluation of the safety or effectiveness of the new animal drug for which approval is sought. 21 CFR § 514.1(b)(8)(iv). All other information includes, but is not limited to, any information derived from other marketing (domestic or foreign) and favorable and unfavorable reports in the scientific literature.

E. Submissions relating to target animal safety, effectiveness, requests for categorical exclusions, labeling, the FOI summary, and all other information should be submitted to the appropriate Division (the Division of Therapeutic Drugs for Non-Food Animals, the Division of Production Drugs, or the Division of Therapeutic Drugs for Food Animals) as determined by the intended uses for the new animal drug. Submissions relating to

Chemistry, Manufacturing, and Controls should be submitted to the Division of Manufacturing Technologies. Environmental assessments and Environmental Impact Statements should be submitted to the Scientific Support Staff in the Office of the Director, ONADE. A submission relating to Human Food Safety (Residue Toxicology, Residue Chemistry, and Microbiology) should be submitted to the Division of Human Food Safety. If a submission is not sent to the appropriate review Division or Staff, processing of the submission may be delayed. Relevant draft labeling, FOI text, and all other information should be submitted with and reviewed concurrently with each technical section. This facilitates the review of the labeling and FOI Summary technical sections.

Submissions to CVM are logged in by the Document Control Unit. Thus, the envelope in which a submission is mailed, or the electronic submission, should be addressed to the Document Control Unit, HFV-199. The cover letter should be directed to the Director of the Division or Staff responsible for the review of the submission.

F. The reviewing Division will notify the sponsor in writing of its conclusions on acceptance or non-acceptance of the data submitted relevant to a technical section. If the reviewing Division finds the data for the technical section to be complete, it will issue a technical section complete letter. A final decision on the approval of an application will be made when the Administrative NADA is submitted and CVM evaluates whether all the data for all technical sections viewed as a whole support approval.

G. Any person intending to file an NADA or a request for an investigational exemption under section 512(j) of the Act is encouraged to request one or more conferences prior to such submission to reach an agreement acceptable to CVM, establishing the submissions or investigations necessary to meet the requirements of 21 CFR 514.1.

H. The synchronizing of major technical sections remains the responsibility of the drug sponsor. There are obvious and varying degrees of cross relationships among major technical sections. For example, concerns about target animal safety may place boundaries on the dose(s) evaluated in drug effectiveness studies.

I. Prior to submission of the NADA, the sponsor is responsible for ensuring all technical sections are compatible and support the approval of the same drug product.

IV. Submitting an Administrative NADA

When a sponsor has received technical section complete letters for each of the technical sections submitted to support approval of a new animal drug, the sponsor may file an Administrative NADA. The Administrative NADA should include a cover letter, signed FDA Form 356V, a table of contents, summary, a copy of each technical section complete letter, complete facsimile labeling, and the FOI summary. The cover letter should be addressed to the Division Director responsible for the evaluation of the target animal safety technical section of the application and should identify at the top of the letter that the submission is an "Administrative NADA."

to CVM to establish an INAD file, or when a major health or environmental effects test is initiated, and ends when an NADA is submitted. The second period (the approval period) begins with submission of the NADA and ends when the application is approved. 35 U.S.C. § 156(g)(4)(B). Subject to certain important limitations, a patent may be extended for a time roughly equal to the second time period plus one half the first time period. 35 U.S.C. § 156(c)(2). Because FDA intends that the time it takes to approve an application that qualifies as an Administrative NADA usually will be shorter than the time it takes to approve a traditional NADA, a new animal drug that was the subject of an Administrative NADA is likely, in most cases, to receive a shorter patent term extension than it would have received had it been the subject of a traditional NADA.